

CLAIMS

What is claimed is:

1. A process for the preparation of a water soluble metallic nanoparticle coated with a mixed monolayer comprising:
 - 5 a) providing a water soluble metallic nanoparticle coated with monolayer of a capture coating component having an affinity for a capture moiety;
 - b) 10 mixing the coated nanoparticle of (a) with a shielding coating component in a mixed solvent, the shielding component having metal binding functionality, the mixed solvent comprising at least one substantially water miscible organic solvent and at least one aqueous solvent wherein the mixed solvent is at a pH of less than 7.0; wherein exchange occurs between the shielding coating component and the capture coating component to form a 15 nanoparticle coated with a mixed monolayer; and
 - c) optionally isolating the mixed monolayer coated metal nanoparticle of (b).
2. A process for the preparation of a water soluble metallic 20 nanoparticle coated with a mixed monolayer comprising:
 - a) providing;
 - i) a metal salt
 - ii) a shielding component having metal binding functionality;
 - 25 iii) a capture coating component having metal binding functionality and having an affinity for a capture moiety;
 - iv) a suitable reducing agent; and
 - v) a mixed solvent comprising at least one substantially 30 water miscible organic solvent and at least one aqueous solvent wherein the mixed solvent is at a pH of less than 7.0;
 - b) 35 mixing elements (i) – (iv) in the mixed solvent of (v) to form a reaction mixture, wherein the final concentration of water in the reaction mixture is from about 9% to about 18% V/V, and wherein a mixed monolayer forms on the metallic nanoparticle; and

- c) optionally isolating the mixed monolayer coated metal nanoparticle of (b).
3. A process for the synthesis of a water soluble metallic nanoparticle coated with a mixed monolayer comprising:
- 5 a) providing a first reaction mixture comprising:
- (i) a metal salt
- (ii) a shielding component having metal binding functionality;
- 10 (iii) a capture coating component having metal binding functionality and having an affinity for a capture moiety;
- (iv) an organic solvent;
- b) providing a second reaction mixture comprising a suitable reducing agent in an aqueous solvent; wherein the second reaction mixture is at a pH of less than 7.0; and
- 15 c) mixing the first and second reaction mixtures wherein the final concentration of water in the mixture is from about 9% to about 18% V/V, and wherein a water soluble metallic nanoparticle coated with a mixed monolayer is
- 20 formed.
4. A process for the preparation of a water soluble metallic nanoparticle coated with monolayer of a capture coating component comprising:
- a) mixing a metal salt with a capture coating component having an affinity for a capture moiety, the capture coating component comprising a metal binding functionality to form a first reaction mixture, wherein the first reaction mixture is at a pH of less than 7.0; and
- 25 b) adding a suitable reducing agent to the first reaction mixture of (a) to form a second reaction mixture comprising metal nanoparticles coated with said capture coating component.
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5. A process according to any of Claims 1-4 wherein the metal of the metallic nanoparticle is selected from the group consisting of; gold,
- 35 silver, platinum, palladium, iridium, rhodium, osmium, iron, copper, cobalt, and alloys composed of these metals.

6. A process according to any of Claims 2-4 wherein the metal salt is selected from the group consisting of HAuCl_4 , AgNO_3 , $\text{Cu}(\text{CH}_3\text{CO}_2)_2$, $\text{Cu}(\text{NO}_3)_2$, HPtCl_6 , and K_2PdCl_4 .

5 7. A process according to any of Claims 1-4 wherein the capture moiety is selected from the group consisting of: peptides, proteins, nucleic acid fragments, collagen, nano-rods, nano-tubes, nano-planes and nano-fibers.

8. A process according to any of Claims 1-4 wherein said capture coating component is selected from the group consisting of

- 10 a) molecules having reactive groups selected from the group consisting of: $-\text{NH}_2$, $-\text{COOH}$, $-\text{CHO}$, $-\text{OH}$, $-\text{X}$ (Cl, Br, I), succinimide, and epoxy groups; and
- b) biomolecules selected from the group consisting of: peptides; tiopronin and GSH.

15 9. A process according to any of Claims 1-4 wherein the metal binding functionality binds metals selected from the group consisting of gold, silver, platinum, palladium, iridium, rhodium, osmium, iron, copper, cobalt, and alloys composed of these metals.

20 10. A process according to any of Claims 1-4 wherein said metal binding functionality is an SH group and said metal is gold.

11. A process according to any of Claims 1-4 wherein said at least one substantially water miscible organic solvent is selected from the group consisting of; C1-C6 alkanols, dimethyl sulfoxide, tetrahydrofuran, dimethylformamide, Dioxane, and acetone

25 12. A process according to any of Claims 1-4 wherein said at least one aqueous based solvent is selected from the group consisting of; water, and acetic acid.

30 13. A process according to any of Claims 1-4 wherein said suitable reducing agent is selected from the group consisting of NaBH_4 , lithium triethylborohydride and hydrogen peroxide.

14. A process according to any of Claims 1-3 wherein said shielding component is selected from the group consisting of short chain ethylene glycol oligomers, ethylene glycol methacrylate, sugars, crown ethers, and acrylamide.

35 15. A process according to Claim 14 wherein said shielding component is a short chain ethylene glycol oligomer.

16. A process according to Claim 15 wherein the short chain ethylene glycol oligomer has a molecular weight less than the entanglement molecular weight.

5 17. A process according to Claim 15 wherein the short chain ethylene glycol oligomer is selected from the group consisting of tetraethylene glycol thiol and diethylene glycol thiol.

18. A process according to Claim 1 wherein after step (b) the metal nanoparticles coated with said capture coating component are optionally isolated and fractionated.

10 19. A process according to any of Claims 1-3 wherein the shielding component comprises at least 50% of the mixed monolayer.

20. A process for the preparation of a water soluble gold nanoparticle coated with a mixed monolayer comprising:

- 15 a) mixing a gold salt with tiopronin, the tiopronin comprising a SH functionality, together in a mixed solvent to form a first reaction mixture, wherein the first reaction mixture is at a pH of less than 7.0, and the mixed solvent is comprised of alcohol and water;
- 20 b) adding NaBH_4 to the first reaction mixture of (a) to form a second reaction mixture comprising gold nanoparticles coated with said tiopronin;
- 25 c) adding short chain ethylene glycol oligomers having an SH functionality wherein a mixed monolayer comprising tiopronin and the short chain ethylene glycol oligomers is formed on the gold particle and the nanoparticle is water soluble; and
- d) optionally isolating the mixed monolayer coated gold nanoparticle of (c).

30 21. A process according to Claim 20 wherein the short chain ethylene glycol oligomer has a molecular weight less than the entanglement molecular weight.

22. A process according to Claim 20 wherein the gold salt is HAuCl_4 .

35 23. A water soluble metal nanoparticle coated with a mixed monolayer, the mixed monolayer comprising a shielding coating component having metal binding functionality, consisting of ethylene glycol

and a capture coating component having a binding functionality for a capture moiety.

24. A water soluble metal nanoparticle of Claim 23 wherein the metal is selected from the group consisting of; gold, silver, platinum,
5 palladium, iridium, rhodium, osmium, iron, copper, cobalt, and alloys composed of these metals.

25. A water soluble metal nanoparticle of Claim 23 wherein the capture moiety is selected from the group consisting of; peptides, proteins, nucleic acid fragments, collagen, nano-rods, nano-tubes, nano-planes and
10 nano-fibers

26. A water soluble metal nanoparticle of Claim 23 wherein said capture coating component is selected from the group consisting of:

- a) molecules having reactive groups selected from the group consisting of: -NH_2 , -COOH , -CHO- , -OH , -X (Cl, Br, I),
15 succinimide, and epoxy groups; and
- b) biomolecules selected from the group consisting of: peptides; tiopronin and GSH.

27. A water soluble metal nanoparticle of Claim 23 wherein the metal is gold and the capture coating component is tiopronin.

28. A water soluble metal nanoparticle of Claim 23 wherein the shielding coating component is a short chain ethylene glycol oligomer.

29. A water soluble metal nanoparticle of Claim 28 wherein the short chain ethylene glycol oligomer has a molecular weight less than the entanglement molecular weight

30. A water soluble metal nanoparticle of Claim 23 wherein the shielding component comprises at least 50% of the mixed monolayer.

31. A process for immobilizing a capture moiety comprising contacting the water soluble metal nanoparticle of Claim 23 with a capture moiety under conditions that permit the binding of the capture moiety to
30 the capture coating component wherein the capture moiety is immobilized.

32. A process according to Claim 30 wherein the metal is gold and the capture coating component is tiopronin and the capture moiety is selected from the group consisting of; proteins and nucleic acids.